PATENT
Attorney Docket No.: 020167-000120US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

GAN, Zhong-Ru

Application No.: 09/423,100

Filed: December 11, 2000

For: CHIMERIC PROTEIN CONTAINING AN INTRAMOLECULAR CHAPERONE-LIKE SEQUENCE AND ITS APPLICATION TO INSULIN PRODUCTION

Customer No.: 20350

Confirmation No.

Examiner: Nichols, Christopher J.

Technology Center/Art Unit: 1647

DECLARATION PURSUANT TO 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Dr. Zhong-Ru Gan, being duly warned that willful false statements and the like are punishable by fine or imprisonment or both, under 18 U.S.C. §1001, and may jeopardize the validity of the patent application or any patent issuing thereon, state and declare as follows:

1. All statements herein made of my own knowledge are true and statements made on information or belief are believed to be true.

2. I am the named inventor of U.S. Patent Application No. 09/423,100.

3. I understand that the Examiner has raised a concern regarding the operability of the claimed invention for first peptidyl fragments shorter than 49 amino acids in length. I present additional data bearing on this question. All the work described herein was either conducted by me, at my direction, or by my colleagues who work with me, as part of the team of scientists working on this project:

In one experiment using recombinant methods, we made a chimeric protein having a shortened first peptidyl sequence of SEQ ID NO1. This chimeric protein lacked the nine C- terminal amino acids of SEQ ID NO1. The chimeric protein was made using the expression vector as generally set forth in Figure 1. This vector, designated P1-2, contains the shortened first peptidyl fragment and mini-proinsulin according to the invention. The expression vector highly expressed miniproinsulin fusion protein in E. coli. The fusion protein refolded correctly with a high efficiency and about as well as that achieved using a first peptidyl fragment having the full amino acid sequence of SEQ ID NO1.

In another experiment, we made a similar chimeric protein having a first peptidyl fragment in which the last 32 C-terminal amino acids of SEQ ID NO:1 were deleted. This first peptidyl fragment was about 17 amino acids in length. This chimeric protein did not succeed in significantly increasing the correct folding of the insulin precursor portion of the chimeric protein.

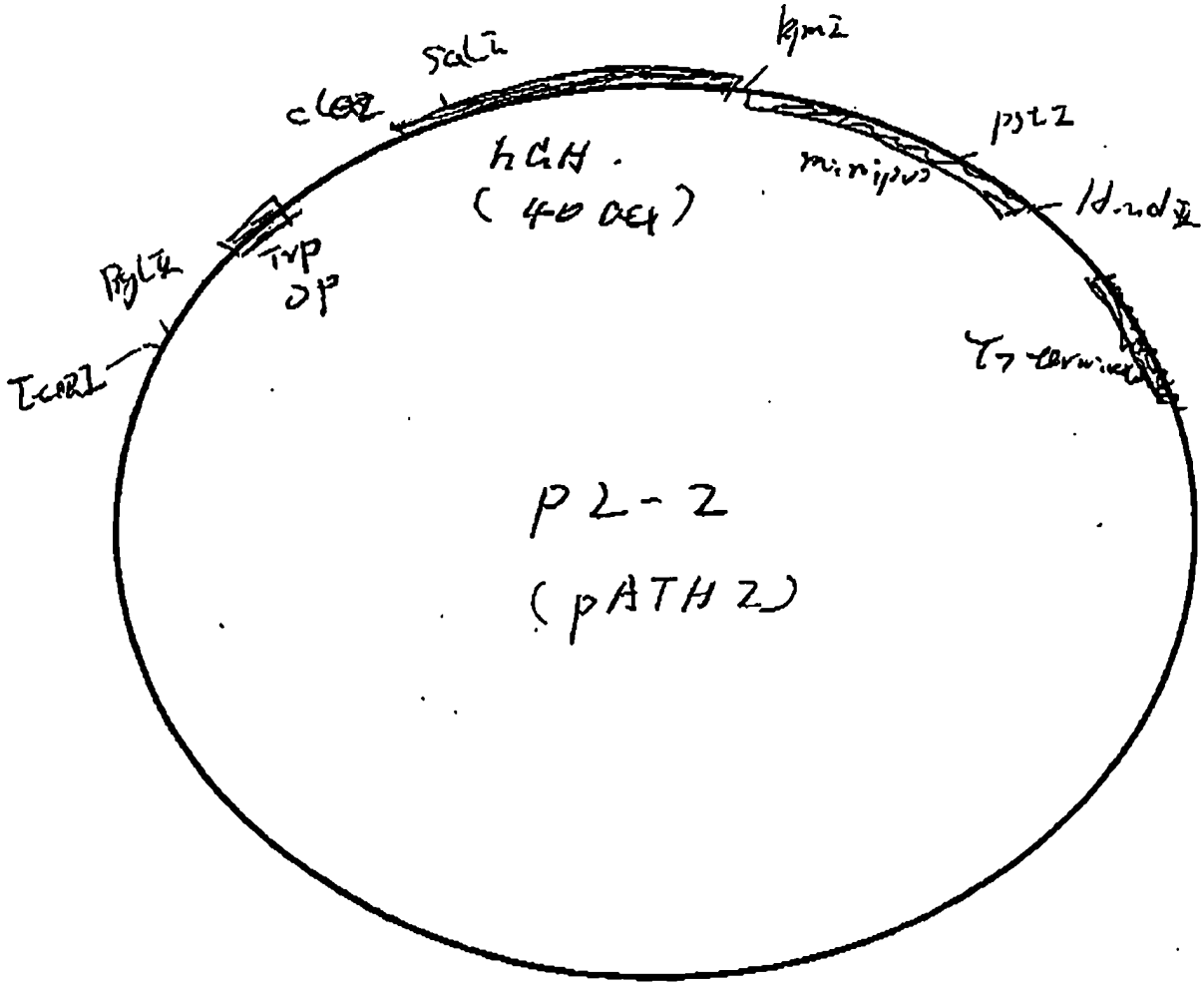
This Declarant has nothing further to say.

Dated: Dec. 3, 2003

Zhong-Ru Gan

Attachment: Figure 1

pL-2.



① SalI - HindIII digest pL-1.
isolate the about ~ 300 bp

② SalI - HindIII digest pLA-76.
Isolate the plasmide.

& colone & ince ②.